

CLAIMS

1. A bispecific antibody that substitutes for the effect of a functional protein.
2. A bispecific antibody that has an activity of functionally substituting for a ligand of a
5 heteromolecule-comprising receptor.
3. The antibody according to claim 2, wherein said heteromolecule-comprising receptor is a dimer.
4. The antibody according to claim 2, wherein said receptor is a cytokine receptor.
5. The antibody according to claim 4, wherein said cytokine receptor is an interferon receptor.
- 10 6. The antibody according to claim 5, wherein said interferon receptor is a type I interferon receptor.
7. The antibody according to claim 6, wherein said type I interferon receptor comprises an AR1 chain and an AR2 chain.
8. The antibody according to claim 7, wherein said antibody functionally substitutes for an
15 interferon which is a ligand of a type I interferon receptor.
9. The antibody according to claim 8, wherein said antibody comprises the variable region of an anti-AR1 chain antibody and the variable region of an anti-AR2 chain antibody.
10. The antibody according to claim 9, wherein said antibody comprises an anti-AR1 chain antibody variable region comprising the amino acid sequence of (a) below and an anti-AR2
20 chain antibody variable region comprising the amino acid sequence of any of the following (b1) to (b10):
 - (a) the H chain variable region amino acid sequence described in SEQ ID NO: 1 and the L chain variable region amino acid sequence described in SEQ ID NO:2;
 - (b1) the H chain variable region amino acid sequence described in SEQ ID NO: 7 and the L
25 chain variable region amino acid sequence described in SEQ ID NO: 8;
 - (b2) the H chain variable region amino acid sequence described in SEQ ID NO: 9 and the L chain variable region amino acid sequence described in SEQ ID NO: 10;
 - (b3) the H chain variable region amino acid sequence described in SEQ ID NO: 19 and the L chain variable region amino acid sequence described in SEQ ID NO: 20;
 - 30 (b4) the H chain variable region amino acid sequence described in SEQ ID NO: 13 and the L chain variable region amino acid sequence described in SEQ ID NO: 14;
 - (b5) the H chain variable region amino acid sequence described in SEQ ID NO: 23 and the L chain variable region amino acid sequence described in SEQ ID NO: 24;
 - (b6) the H chain variable region amino acid sequence described in SEQ ID NO: 5 and the L
35 chain variable region amino acid sequence described in SEQ ID NO: 6;
 - (b7) the H chain variable region amino acid sequence described in SEQ ID NO: 17 and the L

chain variable region amino acid sequence described in SEQ ID NO: 18;

(b8) the H chain variable region amino acid sequence described in SEQ ID NO: 15 and the L chain variable region amino acid sequence described in SEQ ID NO: 16;

(b9) the H chain variable region amino acid sequence described in SEQ ID NO: 21 and the L chain variable region amino acid sequence described in SEQ ID NO: 22;

(b10) the H chain variable region amino acid sequence described in SEQ ID NO: 11 and the L chain variable region amino acid sequence described in SEQ ID NO: 12.

11. The antibody according to claim 9, wherein said antibody comprises an anti-AR1 chain antibody variable region comprising the amino acid sequence of (a) below or an anti-AR2 chain antibody variable region comprising the amino acid sequence of any of the following (b1) to (b3):

(a) the H chain variable region amino acid sequence described in SEQ ID NO: 3 and the L chain variable region amino acid sequence described in SEQ ID NO: 4;

(b1) the H chain variable region amino acid sequence described in SEQ ID NO: 25 and the L chain variable region amino acid sequence described in SEQ ID NO: 26;

(b2) the H chain variable region amino acid sequence described in SEQ ID NO: 9 and the L chain variable region amino acid sequence described in SEQ ID NO: 10;

(b3) the H chain variable region amino acid sequence described in SEQ ID NO: 21 and the L chain variable region amino acid sequence described in SEQ ID NO: 22.

12. A composition comprising the antibody according to any one of claims 2 to 11 and a pharmaceutically acceptable carrier.

13. The composition according to claim 12, wherein said composition is a pharmaceutical composition used for preventing and/or treating viral disease, malignant neoplasm, or immune disease.

14. The composition according to claim 13, wherein said viral disease is a disease that arises and/or progresses as a result of hepatitis C virus infection.

15. The composition according to claim 14, wherein the disease that arises and/or progresses as a result of hepatitis C virus infection is acute or chronic hepatitis C, cirrhosis, or liver cancer.

16. The composition according to claim 13, wherein said viral disease is a disease that arises and/or progresses as a result of hepatitis B virus infection.

17. The composition according to claim 16, wherein the disease that arises and/or progresses as a result of hepatitis B virus infection is acute or chronic hepatitis B, cirrhosis, or liver cancer.

18. The composition according to claim 13, wherein the malignant neoplasm is chronic myelocytic leukemia, malignant melanoma, multiple myeloma, renal cancer, gliosarcoma, medulloblastoma, astrocytoma, hairy cell leukemia, AIDS-related Kaposi's sarcoma, skin T lymphoma, or non-Hodgkin's lymphoma.

19. The composition according to claim 13, wherein the immune disease is multiple sclerosis.
20. A method for preventing and/or treating viral disease, malignant neoplasm, or immune disease, comprising the step of administering the antibody according to any one of claims 2 to 11, or the composition according to any one of claims 12 to 19.
- 5 21. Use of the antibody according to any one of claims 2 to 11 for producing the composition according to any one of claims 12 to 19.
22. A kit used in the method of preventing and/or treating diseases according to claim 20, wherein said kit comprises at least the antibody according to any one of claims 2 to 11, or the composition according to claim 12.
- 10 23. An antibody recognizing both an enzyme and a substrate thereof, wherein said antibody is a bispecific antibody which functionally substitutes for a cofactor that enhances the enzymatic reaction.
24. The antibody according to claim 23, wherein said enzyme is a proteolytic enzyme.
25. The antibody according to claim 24, wherein said proteolytic enzyme, substrate, and cofactor
- 15 are blood coagulation/fibrinolysis associated factors.
26. The antibody according to claim 25, wherein the enzyme of a blood coagulation/fibrinolysis associated factor is blood coagulation factor IX and/or activated blood coagulation factor IX; the substrate is blood coagulation factor X; and the cofactor is blood coagulation factor VIII and/or activated blood coagulation factor VIII.
- 20 27. The antibody according to any one of claims 23 to 26, wherein said antibody comprises a complementarity determining region comprising the amino acid sequence of anti-blood coagulation factor IX/IXa antibody CDR3 of the following (a1) or (a2) or a complementarity determining region functionally equivalent thereto, and a complementarity determining region comprising the amino acid sequence of anti-blood coagulation factor X antibody CDR3
- 25 described in any one of the following (b1) to (b9) or a complementarity determining region functionally equivalent thereto:
- (a1) H chain CDR3 amino acid sequence described in SEQ ID NO: 42;
- (a2) H chain CDR3 amino acid sequence described in SEQ ID NO: 46;
- (b1) H chain CDR3 amino acid sequence described in SEQ ID NO: 50;
- 30 (b2) H chain CDR3 amino acid sequence described in SEQ ID NO: 54;
- (b3) H chain CDR3 amino acid sequence described in SEQ ID NO: 58;
- (b4) H chain CDR3 amino acid sequence described in SEQ ID NO: 62;
- (b5) H chain CDR3 amino acid sequence described in SEQ ID NO: 66;
- (b6) H chain CDR3 amino acid sequence described in SEQ ID NO: 70;
- 35 (b7) H chain CDR3 amino acid sequence described in SEQ ID NO: 74;
- (b8) H chain CDR3 amino acid sequence described in SEQ ID NO: 78;

(b9) H chain CDR3 amino acid sequence described in SEQ ID NO: 82.

28. The antibody according to any one of claims 23 to 26, wherein said antibody comprises a complementarity determining region comprising the amino acid sequences of anti-blood coagulation factor IX/IXa antibody CDR of the following (a1) or (a2) or a complementarity
5 determining region functionally equivalent thereto, and a complementarity determining region comprising the amino acid sequence of anti-blood coagulation factor X antibody CDR described in any one of the following (b1) to (b9) or a complementarity determining region functionally equivalent thereto:

(a1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 40, 41, and 42,
10 respectively;

(a2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 44, 45, and 46, respectively;

(b1) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 48, 49, and 50, respectively;

15 (b2) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 52, 53, and 54, respectively;

(b3) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 56, 57, and 58, respectively;

(b4) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 60, 61, and 62,
20 respectively;

(b5) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 64, 65, and 66, respectively;

(b6) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 68, 69, and 70, respectively;

25 (b7) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 72, 73, and 74, respectively;

(b8) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 76, 77, and 78, respectively;

(b9) H chain CDR 1, 2, and 3 amino acid sequences described in SEQ ID NOs: 80, 81, and 82;
30 respectively.

29. A composition comprising the antibody according to any one of claims 23 to 28 and a pharmaceutically acceptable carrier.

30. The composition according to claim 29, wherein said composition is a pharmaceutical composition used for preventing and/or treating bleeding, disorder accompanied by bleeding, or
35 disorder caused by bleeding.

31. The composition according to claim 30, wherein the bleeding, disorder accompanied by

bleeding, or disorder caused by bleeding is a disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII.

5 32. The composition according to claim 31, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is hemophilia A.

10 33. The composition according to claim 31, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is a disorder in which an inhibitor against blood coagulation factor VIII and/or activated blood coagulation factor VIII is generated.

34. The composition according to claim 31, wherein the disorder that arises and/or progresses as a result of an activity decrease or deficiency of blood coagulation factor VIII and/or activated blood coagulation factor VIII is acquired hemophilia.

15 35. The composition according to claim 31, wherein the disorder that arises and/or progresses as a result of an activity decrease of blood coagulation factor VIII and/or activated blood coagulation factor VIII is von Willerbrand's disease.

20 36. A method for preventing and/or treating bleeding, disorder accompanied by bleeding, or disorder caused by bleeding, wherein said method comprises the step of administering the antibody according to any one of claims 23 to 28, or the composition according to any one of claims 29 to 35.

37. Use of the antibody according to any one of claims 23 to 28 for preparing the composition according to any one of claims 29 to 35.

25 38. A kit used in the method of preventing and/or treating disorders according to claim 36, wherein said kit comprises at least the antibody according to any one of claims 23 to 28 or the composition according to claim 29.